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On May 28, 2002

TOWNSEND and TOWNSEND and CREW LLP

By: Masha M. Martinenko
Masha M. Martinenko

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

GAN, Zhong-Ru

Application No.: 10/054,873

Filed: January 22, 2002

For: CHIMERIC PROTEIN CONTAINING AN INTRAMOLECULAR CHAPERONE-LIKE SEQUENCE

Examiner: Not yet assigned

Art Unit: 1647

COMMUNICATION UNDER 37 C.F.R. §§ 1.821-1.825 AND PRELIMINARY AMENDMENT

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Sir:

In response to the request to comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, that accompanied the Notice to File Corrected Application Papers mailed February 26, 2002, Applicants submit herewith the required paper copy and computer readable copy of the Substitute Sequence Listing. Please amend the specification in adherence with 37 C.F.R. §§ 1.821-1.825 as follows.

In the Specification:

Please replace the paragraph beginning at page 12, line 29, with the following:

--In a preferred embodiment, the present invention provides a chimeric protein described above, wherein the second peptidyl fragment consists of the amino acid sequences of SEQ ID NO:3.--

Please replace the paragraph beginning at page 20, line 9, with the following:

--In a preferred embodiment, the present invention provides a process for obtaining a correctly folded insulin-precursor-containing chimeric protein described above, wherein the cleavable amino acid residue is an Arg or a Lys residue. Also preferably, the cleavable amino acid residues consist of the amino acid sequence of SEQ ID NO:3.--

Please replace the paragraph beginning at page 23, line 27, with the following:

--A DNA fragment encoding the hGH-mini-proinsulin consisting of the amino acid sequence of SEQ ID NO:6 was chemically synthesized according to the procedure disclosed in Gan et al., *Gene*, 1989, 79:159-166. A 5' Cla I site and a 3' Hind III site were included in the synthesized DNA fragment. Briefly, a fragment from the 5' Cla I to 3' Kpn I, which cuts the nucleotide sequence encoding amino acid residues 51 and 52 of the SEQ ID NO:6, and a fragment from 5' Kpn I to 3' Hind III were chemically synthesized and subcloned into a pUC18 vector, respectively. Subsequently, the DNA fragment encoding the entire amino acid sequence of SEQ ID NO:6 was subcloned into a modified pATH2 vector such that expression of the hGH-mini-proinsulin was under the control of a Trp promoter and a SD sequence. The resulting vector, pZRhi-1 (Figure 2) was used to express the hGH-mino proinsulin fusion protein.--

Please cancel the present "SEQUENCE LISTING", pages 27-31, and insert therefor the accompanying paper copy of the Substitute Sequence Listing, page numbers 1 to 5, at the end of the application. Cancel the page numbers for the Claims and Abstract and renumber, accordingly.

REMARKS

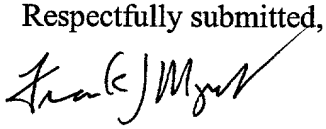
Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-7, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

Attached hereto is a marked-up version of the changes made to the Specification by the current Amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 29 of page 12 has been amended as follows:

In a preferred embodiment, the present invention provides a chimeric protein described above, wherein the second peptidyl fragment consists of the amino acid sequences ~~sequence~~ of SEQ IDNO:3 ~~SEQ ID:3~~.

Paragraph beginning at line 9 of page 20 has been amended as follows:

In a preferred embodiment, the present invention provides a process for obtaining a correctly folded insulin-precursor-containing chimeric protein described above, wherein the cleavable amino acid residue is an Arg or a Lys residue. Also preferably, the cleavable amino acid residues consist of the amino acid sequence of SEQ ID NO:3 ~~SEQ ID:3~~.

Paragraph beginning at line 27 of page 23 has been amended as follows:

A DNA fragment encoding the hGH-mini-proinsulin consisting of the amino acid sequence of SEQ ID NO:6 was chemically synthesized according to the procedure disclosed in Gan et al., *Gene*, 1989, 79:159-166. A 5' Cla I site and a 3' Hind III site were included in the synthesized DNA fragment. Briefly, a fragment from the 5' Cla I to 3' Kpn I, which cuts the nucleotide sequence encoding amino acid residues 51 and 52 of the SEQ ID NO:6, and a fragment from 5' Kpn I to 3' ~~3'~~ Hind III were chemically synthesized and subcloned into a pUC18 vector, respectively. Subsequently, the DNA fragment encoding the entire amino acid sequence of SEQ ID NO:6 ~~SEQ ID:6~~

was subcloned into a modified pATH2 vector such that expression of the hGH-mini-proinsulin was under the control of a Trp promoter and a SD sequence. The resulting vector, pZRhi-1 (Figure 2) was used to express the hGH-mino proinsulin fusion protein.